IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BIOVAIL LABORATORIES INTERNATIONAL SRL a corporation of Barbados, Plaintiff, v. ANDRX PHARMACEUTICALS, LLC and ANDRX CORPORATION, Defendants.	)	C.A. Nos. 05-586 (GMS) 05-730 (GMS) 06-620 (GMS) (CONSOLIDATED)

BIOVAIL'S ANSWERING CLAIM CONSTRUCTION BRIEF

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INTRODUCTION

Andrx's arguments in support of its claim construction are largely conclusory and almost entirely unsupported by any evidence whatsoever -- whether intrinsic or extrinsic. Andrx ignores the plain and ordinary language of the '791 and '866 patent claims, incessantly reads extraneous limitations into the claims, and injects infringement and validity arguments into its analysis. Extrinsic evidence, including dictionaries and other sources, become primary claim construction tools in Andrx's flawed analysis, rather than the disfavored tools they are. In addition, Andrx improperly asks the Court to make factual findings in the context of the Court's claim construction analysis as to the meanings and interpretations of various technical documents used by persons of ordinary skill in the art, including the USP and FDA guidance documents.

Biovail, on the other hand, offers constructions that derive from the plain language of the claims and are firmly grounded on well-established claim construction principles. Biovail does not ask the Court to read extraneous limitations into the '791 or '866 patent claims or ask the Court to make factual findings in the guise of claim construction.[1]

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[1] Although irrelevant to claim construction, Andrx opens its brief with the unfounded assertion that the present litigation has kept its proposed generic products "out of the market." [D.I. 146, p. 1.] This is incorrect. Andrx's own actions have kept it out of the market. Within a month after Biovail filed this lawsuit, the FDA placed Andrx on Official Action Indicated (OAI) status for violations of current Good Manufacturing Practices -- standards for the control and management of manufacturing and quality testing of pharmaceuticals products. While under OAI status, the FDA will not approve any Andrx generic drug application, including the one at issue here. Andrx has yet to correct its manufacturing problems to the satisfaction of the FDA.

LEVEL OF ORDINARY SKILL IN THE ART

Claims must be interpreted from the perspective of a person of ordinary skill in the art as of the patent's effective filing date. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005). For the '791 patent that date is no later than June 26, 1991. For the '866 patent, that date is no later than December 10, 1999.

The '791 patent is directed to novel extended-release formulations of the drug diltiazem. As such, a person of ordinary skill in the art to which the '791 patent is directed would have at least a Bachelor's degree in pharmaceutical sciences or an analogous field such as, chemistry, chemical engineering, or biology, and two years of industrial formulation experience.

The '866 patent is directed to novel chronotherapeutic formulations of the drug diltiazem. As such, persons of ordinary skill in the art to which the '866 patent is directed would, from a formulation perspective, have at least a Bachelor's degree in pharmaceutical sciences or an analogous field such as, chemistry, chemical engineering, or biology, and two years of industrial formulation experience. From a pharmacokinetic perspective, they would have at least a Bachelor's degree in pharmacy or an analogous field such as, pharmacology, pharmaceutical sciences, chemistry, chemical engineering, or biology, and at least two years of experience in clinical pharmacology or clinical practice.

ARGUMENT

A. THE PROPER CONSTRUCTION OF THE '791 PATENT CLAIMS

The main dispute as to the '791 patent is whether the claims are limited to the composition (pharmaceutical product) in the dry state, *i.e.*, prior to ingestion, or extends to the form of the composition *in vivo*, *i.e.*, after exposure to pH conditions of the gastrointestinal tract. As explained below, Andrx relies heavily on a prior construction of a different district court that is: (a) not controlling precedent because the Federal Circuit did not adopt its construction, and (b) not persuasive authority because it was based on a misguided and flawed claim construction analysis. In addition, Andrx improperly seeks to have the Court decide infringement under the guise of claim construction. The Federal Circuit has made plain that claim construction and infringement are separate issues. *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996); *see also Takata Corp. v. AlliedSignal Inc.*, No. 98-94 (MMS), 1999 U.S. Dist. LEXIS 15037, *29 n. 15 (D. Del. Aug. 19, 1999) ("The Federal Circuit Court of Appeals has consistently rejected the consideration of such [invalidity and non-infringement] argument[s] at the claim construction stage and continues to draw a line between claim construction issues and issues of infringement and invalidity. . . . The Court will not consider the merits of any such arguments while engaging in claim construction." (internal citations omitted)).

1. "extended-release galenical composition"

'791 Claim Terms	Biovail's Construction	Andrx's Construction
"extended-release galenical composition"	a pharmaceutical composition that releases the active ingredient over an extended period of time.	This limitation means a pharmaceutical composition as it is prepared in the dry state and before ingestion by a patient, that releases the active ingredient over an extended period of time.

Andrx's construction of the term "extended-release galenical composition," like its other proposed constructions, is crafted to support its argument that the '791 claims are directed to a composition in the dry state. Andrx asserts, without any support whatsoever, that the term "galenical composition" means a composition in its dry, finished pharmaceutical form. [D.I. 146, p. 6.] Nowhere in the patent or the prosecution history is the term "galenical composition" limited to the dry state, and Andrx has cited no intrinsic or extrinsic evidence in support of its position.

Instead, Andrx argues that by 1991 the term galenical "had been used in a number of patents." [D.I. 146, p. 6.] Indeed, it had been. In such patents, galenical is used as an umbrella term covering all types of pharmaceuticals. For example, U.S. Patent No. 4,032,637 concerns "solid ***or liquid*** galenical preparations for oral, rectal or parenteral administration, e.g. tablets, capsules, dragees [medicated candies], ***drop solutions***, ***syrups***, suppositories or ***sterile solutions***." [21 A-857 (2:47-50) (emphasis added); *see also* 22 A-862, U.S. Patent No. 4,336,263 (5:40-43) and 23 A-870, U.S. Patent No. 4,018,933.]

Andrx also asserts that "as a matter of logic" once the galenical composition is ingested it can no longer be a galenical composition as required by the '791 claims because, in its view, when the composition is exposed to digestive fluids, the "at least a water-soluble polymer" of the microporous membrane would dissolve, and the composition would lack a required element. Andrx's argument is unsupported and improper in the context of the Court's claim construction analysis. *Takata Corp.*, 1999 U.S. Dist. LEXIS at *29 n.15 ("The Court will not consider the merits of any such [invalidity or infringement] arguments while engaging in claim construction.").

Although not relevant to claim construction, in fact, when the water-soluble polymer is exposed to digestive fluids in beads made according to the '791 claims, it does not entirely dissolve from the membrane.

Andrx also points to Claim 3 of the '791 patent as support for its construction. Andrx asserts that it would be impossible to determine if a claimed composition contained the required "about 8%" by weight of the wetting agent post-ingestion. Not only is this attorney argument unsupported and based on conjecture, but here again, Andrx simply is trying to inject a non-infringement argument to bolster its asserted construction. Further, to the extent that Andrx is trying to somehow add limitations to Claim 1 by using Claim 3, this is improper.

Finally, Andrx asserts that it has not found any reference in which a solid oral dosage form contained as an ingredient "any type of gastric fluid or other bodily fluid." [D.I. 146, p. 7.] Andrx's argument misses the point. The '791 patent compels an *in vivo* construction because key to the invention is the admixture of diltiazem and wetting agent that keeps diltiazem in a dissolved (or liquid) state after the composition is exposed to pH conditions of the gastrointestinal tract. [6 A-88.] Biovail's construction does not require that gastric fluid or any other bodily fluid be an ingredient of the composition.

2. "beads"

'791 Claim Terms	Biovail's Construction	Andrx's Construction
"beads"	the structure wherein the wetting agent is in admixture with one or more diltiazem salts to maintain the solubility of the diltiazem when the composition is exposed to pH conditions of the gastrointestinal tract or other adverse conditions the composition will meet *in vivo*.	This limitation refers to the dry, uncoated material that is subsequently coated with a microporous membrane to form the galenical composition referred to in the claim.

Andrx's construction of the term "beads" likewise is crafted to support its argument that the '791 claims are directed to a composition in the dry state. Andrx relies on selected passages from the patent specification that describe how beads of an embodiment of the invention are manufactured to argue that the term "beads" should be limited to the dry state. [D.I. 146, pp. 8-9.] This is an attempt to read limitations from the specification into the claims, which is improper. *See Phillips*, 415 F.3d at 1323 (courts must "avoid the danger of reading limitations from the specification into the claims.") Of course, these portions of the specification, describing how beads are first manufactured (or first come into existence) have nothing to do with the relevant question of when the beads cease to be beads. The plain language of the claims provides the answer and establishes that there will be "beads" containing diltiazem salts and wetting agent in the soluble (or dissolved) state after the formulation is exposed to pH conditions of the gastrointestinal tract:

> . . . an effective amount of wetting in admixture with the one or more Diltiazem salts to maintain the solubility of the Diltiazem ***in each bead***, ensuring that the solubility of the Diltiazem ***is unaffected by the pH of the gastrointestinal tract*** or other adverse conditions which the composition will meet . . . . [1 A-7 (8:63-9:1) (emphasis added).]

As explained in Biovail's opening brief [D.I. 147, p. 4], the need to keep diltiazem in a dissolved state only arises when the formulation is in pH conditions of the gastrointestinal tract, and of course only arises when the diltiazem is already dissolved. Thus, the phrase "maintain the solubility of the Diltiazem in each bead," clearly contemplates that beads will contain dissolved diltiazem.

Andrx also asserts that the prosecution history supports its construction.

In doing so, Andrx strings together a number of passages from the inventors' May 28, 1993 submission, resulting in a misleading interpretation of that submission. Andrx first cites to the following paragraph:

> Thus, at the outset, it is noted that the present composition is characterized by the use of beads consisting essentially of in admixture together an effective amount of Diltiazem or one of more salts thereof as an active ingredient and the wetting agent as defined in the claims. The beads are also coated with a microporous membrane as defined in the claims. [5 A-71.]

Nothing in this passage precludes an *in vivo* construction. Moreover, Andrx omits the very next paragraph which makes plain that the beads exist *in vivo* -- clarifying that the purpose of the admixture (which is contained within the beads) is to keep diltiazem dissolved after the composition is exposed to pH conditions of the gastrointestinal tract:

> In essence, in admixture, the wetting agent appears to control, or strongly influence, the solubility of Diltiazem and does not permit this solubility to be affected by pH or other adverse conditions in the gastrointestinal tract. Further, this control appears to occur within the core of Diltiazem and wetting agent. This control affords a gradual release of Diltiazem in a relatively uniform manner over a period of about 24 hours. . . . [5 A-71.]

Next, Andrx asserts that the inventors distinguished the Debregeas patent by somehow disclaiming the type of beads that Andrx uses. Andrx is wrong. The inventors distinguished the very specific disclosure of Debregeas on two separate grounds. One ground was to point out that Debregeas used a different manufacturing process than that disclosed in the '791 patent, thus the inventors' statement that "[c]learly, it is impossible to have a sugar central core in a homogeneous bead as in the present invention. Such a bead is, by nature, heterogeneous." [5 A-74.] This statement

viewed in context is merely an attempt to distinguish Debregeas based on process or manufacturing differences, and had nothing to do with defining or limiting the terms "beads" or "wetting agent." This is clarified by the remainder of the inventors' argument, which Andrx fails to cite:

> . . . the galenical Diltiazem preparation described by [Debregeas] clearly does not disclose a Diltiazem bead composition containing a wetting agent, ***prepared by the extrusion spheronization process***. Such a bead composition is necessarily a homogeneous bead composition. [5 A-73 (emphasis added).]

Distinguishing a manufacturing process employed in the invention from that employed in Debregeas does not shed any light on the question of the function and definition of the term "beads" or "wetting agent." In particular, it does not contradict the clear description provided of the *in vivo* function of the wetting agent from this same response:

> . . .Debregeas et al does not disclose saccharose as a wetting agent. The saccharose contained in the central core of the ***bead*** cannot act as a wetting agent because in order to do so the saccharose must be mixed with the Diltiazem and, therefore, saccharose ***must be in solution*** with Diltiazem. Unfortunately, in this system saccharose can only end up in solution after all the layers of Diltiazem are dissolved. In other words, saccharose can only become effective when there is not longer a need therefor. [5 A-76-77 (emphasis added).]

Further, the words "must be in solution" above mandate an *in vivo* construction of the '791 patent claims because they make clear that, despite how the composition is initially manufactured, the wetting agent and diltiazem "must be in solution" for the wetting agent to perform its intended purpose, *i.e.*, to keep diltiazem in solution. This solution only occurs *in vivo* (*i.e.*, after exposure to pH conditions of the gastrointestinal tract), and not in the dry, pre-ingested beads. The inventors clearly

distinguished Debregeas, in this passage based on the fact that *in vivo*, the wetting agent will never exist in solution with the diltiazem in the Debregeas system. If an *in vivo* construction were irrelevant, as Andrx asserts, there would be no reason to distinguish Debregeas based on its *in vivo* performance.

3. "each bead"

'791 Claim Terms	Biovail's Construction	Andrx's Construction
"each bead"	refers to the beads containing an effective amount of one or more of said Diltiazem salts as the active ingredient. This term does not require that every single bead of the composition contain diltiazem salt and wetting agent in admixture.	The "each bead" limitation requires that every single bead must contain diltiazem salt and wetting agent in admixture.

Andrx's construction requires that every single bead in the composition contain an admixture of diltiazem and wetting agent, and expressly rules out the possibility that the composition contain other beads that do not contain diltiazem, such as cushioning beads (beads that do not contain drug, but are used for example to help protect the integrity of the drug-containing beads when they are compressed into a tablet).

Andrx's construction is not based on the plain and ordinary language of the claims, but instead seeks to improperly read limitations into the claims from the patent specification and even the prosecution history. For example, Andrx points to Examples 1 and 2 of the '791 patent and Mr. Deboeck's declaration to the Patent Office describing an embodiment of his invention as support that every single bead of the claimed formulations must contain diltiazem salt and wetting agent in admixture. [D.I. 146, p. 12.] The fact that these **examples** employ one type of bead, *i.e.*, a bead containing diltiazem salts and a wetting agent, does not mean the '791 patent claims are

so limited. It is improper to limit a claim term to the embodiments disclosed and described in the specification or prosecution history. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1312, 1323 (Fed. Cir. 2005) (*en banc*) ("The written description part of the specification itself does not delimit the right to exclude. That is the function and purpose of the claims," and courts must "avoid the danger of reading limitations from the specification into the claims.").

Further, Andrx misses the point with the cases it cites at page 13 of its brief. [D.I. 146, p. 13.] Biovail does not dispute that the term "each" means "each and every." But the term "each" clearly modifies and refers to the beads defined in the preceding phrase of the claim, *i.e.*, those beads "containing an effective amount of one or more of said Diltiazem salts as the active ingredient." Each one of these beads must also contain an "effective amount of a wetting agent." However, nothing about this use of the term "each" precludes the possibility of having beads in the composition that do not contain diltiazem at all.

As Biovail explained in its opening brief [D.I. 147, pp. 21-22], the plain language of the claims provide that the composition "comprises" beads containing an effective amount of one or more of said diltiazem salts as the active ingredient. Because of the use of the open-ended term "comprises," the formulation may also include other types of beads, *e.g.*, cushioning beads, that are not required to contain one or more diltiazem salts. *See AFG Indus., Inc. v. Cardinal IG Co., Inc.*, 239 F.3d 1239, 1244-45 (Fed. Cir. 2001) ("We have consistently held that the word 'comprising' is an open transition phrase" and that "its scope may cover devices that employ additional, unrecited elements."). Thus, when the claim refers to "each bead," it refers to the particular beads

mentioned, *i.e.*, beads containing and effective amount of one or more of said diltiazem salts as the active ingredient.

4. "an effective amount of wetting agent"

'791 Claim Terms	Biovail's Construction	Andrx's Construction
"an effective amount of wetting agent"	an amount of wetting agent sufficient to maintain the solubility of the diltiazem in each bead, ensuring that the solubility of the diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein.	An effective amount of wetting agent means an amount of wetting agent that acts within each bead to maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein as further required by the claim language.

Andrx's construction and arguments in support of its construction are unclear and not understood. Indeed, Andrx's argument that the claims are limited to a composition in the dry state appears to completely break down when Andrx gets to this element of the claim. Andrx concedes, as it must, that whether the amount of wetting agent is "an effective amount," depends on whether it exists in an amount sufficient to "maintain the solubility of the Diltiazem in each bead, ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract. . . ." [D.I. 146, p. 14.] Thus, under Andrx's own construction, one will not know whether the wetting agent exists in an "effective amount" until one verifies that the solubility of the diltiazem is unaffected in conditions that represent the *in vivo* environment of the gastrointestinal tract. The only way to know this is to observe how the bead functions in these *in vivo* conditions, *i.e.*, after exposure to pH conditions of the gastrointestinal tract. Analysis of the bead in only the dry, pre-ingested state will not permit one to determine whether it

meets the claim construction Andrx advances.[2]

5. "admixture"

'791 Claim Terms	Biovail's Construction	Andrx's Construction
"admixture"	Means a homogeneous admixture of one or more diltiazem salts and wetting agent can be found at a point in time during the life of the compositions, in particular during their *in vivo* transit from the stomach to the less acidic environment of the intestinal tract. Thus, a formulation will satisfy the admixture language of the '791 patent claims if the formulation is exposed to pH conditions that are found in the gastrointestinal tract, and operates such that beads of the formulation include a homogeneous admixture of one or more diltiazem salts and wetting agent in those conditions. The term homogeneous means having one or more salts of diltiazem and wetting agent throughout the admixture of one or more salts of diltiazem and wetting agent.	Admixture means two or more items that are commingled and interdispersed to obtain a homogeneous product (in this case, bead). In addition, the claim language "each bead containing . . . wetting agent in admixture with the one or more diltiazem salts" requires that the entirety of the bead be homogeneous. The term "homogeneous" means that samples taken anywhere within the bead have identical compositions. Admixture should be read to refer to the dried, uncoated bead that is subsequently coated with a microporous membrane and included in the galenical composition.

Andrx's construction of the term "admixture" is incorrect for several reasons. First, Andrx relies heavily on the district court's opinion in a prior litigation

[2] To the extent that Andrx argues for some other limitations to be read into this claim, those arguments are unclear. To the extent that Andrx seeks to add a limitation to the claims whereby it is the wetting agent, and the wetting agent alone, that maintains the solubility of diltiazem (to the exclusion of any other factor that may contribute to the solubility), there is no support for such a limitation. Also, to the extent that Andrx seeks to add a geographical limitation to the claims, whereby at every point inside the bead and at no point outside the bead the wetting agent keeps diltiazem in a dissolved state, there is likewise no support for such a limitation.

involving different products for support for its construction. [D.I. 146, pp. 16-19.] That non-precedential district court opinion, however, was misguided and flawed. For example, the district court limited the '791 patent claims to the dry state based on portions of the patent specification where the inventors described two methods of manufacturing beads according to the invention. *Biovail Corp. v. Andrx Pharms., Inc.*, 158 F. Supp. 2d 1318, 1321-1323 (S.D. Fla. 2000). However, these portions of the specification are uninformative on the meaning of the term "admixture," because they only describe how to manufacture a bead. Indeed, for all of the reasons stated above, the term "admixture" focuses on the performance of the wetting agent in solution with diltiazem *in vivo*. Moreover, in construing the term "wetting agent," the district court ignored the plain language of the claims and prosecution history, and adopted a definition of "wetting agent" based solely on expert testimony. *Id.* at 1325. While courts are always free to rely on experts to explain the technology at issue, expert testimony as to the meaning of claim terms is a most disfavored form of extrinsic evidence. *Vitronics Corp.*, 90 F.3d at 1584-85. Indeed, so misled was the district court by this extrinsic evidence that it held that sugar is not a wetting agent when in solution with Diltiazem, despite the plain language of claims and prosecution history identifying sugar as a wetting agent. *Biovail*, 158 F. Supp. 2d at 1326. In fact, even Andrx no longer disputes that sugar is a "wetting agent." [D.I. 142, Exh. A, p. 2.]

The Federal Circuit did not adopt these erroneous constructions, and expressly left open the possibility of an *in vivo* claim construction:

> This court also need not determine whether claim 1 of the '791 patent is limited to the product in its dry state or extends to the form of the product *in vivo*, because the outcome of this case does not turn on that issue. *Biovail*

> *Corp. v. Andrx Pharms., Inc.*, 239 F.3d 1297, 1301 (Fed. Cir. 2001).

Andrx's assertion that the Federal Circuit was "quite skeptical" of an *in vivo* construction is baseless and plainly inconsistent with the Federal Circuit opinion.[3]

Andrx (citing the inventors' May 28, 1993 submission to the Patent Office) relies on the same passages from the prosecution history discussed above regarding *manufacturing* differences between the claimed beads and the beads of Debregeas for the broad proposition that Biovail is estopped from arguing that depositing diltiazem on a sugar sphere creates an admixture. [D.I. 146, pp. 17-18.]

As discussed above, the distinction drawn regarding the manufacturing processes of the claimed invention compared to Debregeas does not detract from the clear discussion in this same response clarifying that the crucial time when the admixture must exist between the diltiazem and wetting agent is when the two substances are in solution, which of course only occurs *in vivo* (*i.e.*, after exposure to pH conditions of the gastrointestinal tract):

> . . . Debregeas does not disclose saccharose as a wetting agent. The saccharose contained in the central core of the ***bead*** cannot act as a wetting agent because in order to do so the saccharose ***must be mixed with*** the Diltiazem and,

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[3] Andrx also improperly injects infringement arguments into the claim construction analysis by suggesting that its proposed products are similar to Debregeas. These arguments should be disregarded. *Takata Corp.*, 1999 U.S. Dist. LEXIS at *29 n. 15 ("The Federal Circuit Court of Appeals has consistently rejected the consideration of such [invalidity and non-infringement] argument[s] at the claim construction stage and continues to draw a line between claim construction issues and issues of infringement and invalidity. … The Court will not consider the merits of any such arguments while engaging in claim construction." (internal citations omitted)). At the appropriate time, Biovail will present expert evidence and testimony from Andrx's own witnesses demonstrating that Andrx's proposed products and Debregeas are significantly different.

> therefore, saccharose ***must be in solution*** with Diltiazem. Unfortunately, in this system saccharose can only end up in solution after all the layers of Diltiazem are dissolved. In other words, saccharose can only become effective when there is not longer a need therefor. [2 A-21 (June 22, 1992 Amendment, p. 13) (emphasis added).]

Further, Andrx's construction requires that the entirety of the bead be homogeneous. Despite its representation, Andrx's construction is inconsistent with the Federal Circuit's construction of the term admixture. The Federal Circuit held that the "***admixture*** of diltiazem salt and wetting agent that comprises the bead of claim 1 of the '791 patent must be homogeneous," and not that the bead must be homogeneous. *Biovail*, 239 F.3d at 1302 (emphasis added). Thus, "homogeneous admixture" requires only that wherever there exists diltiazem salt within the bead, it must exist in a homogeneous admixture with the wetting agent.[4]

6. "to maintain the solubility of the Diltiazem in each bead"[5]

'791 Claim Terms	Biovail's Construction	Andrx's Construction
"to maintain the solubility of the	Means the wetting agent does not permit the solubility of the	This limitation requires that the numerical value of the solubility of the

[4] As best understood by Biovail, Andrx seems to be arguing that if, for example, a bead contains a homogeneous solution of diltiazem and wetting agent with air pockets or bubbles within the bead, then under Andrx's construction, the bead would fall outside the '791 claims because it contains only "localized homogeneity," *i.e.*, the air bubble would not be a homogeneous admixture of diltiazem and wetting agent. Under Biovail's construction, regardless of the existence of air pockets or air bubbles, the bead would fall inside the '791 claims because everywhere within the bead that diltiazem is found, there is also wetting agent in a homogeneous mixture with the diltiazem.

[5] Biovail reprints Andrx's construction as it is set forth in the Final Joint Claim Construction Chart. In its opening claim construction brief, Andrx's construction for the claim term adds the word "given" to the phrase "dissolved in a *given* amount of solvent."

Diltiazem in each bead"	diltiazem to be affected by the pH or other adverse conditions of the gastrointestinal tract in a manner that would prevent a gradual release of the drug in a relatively uniform manner. The term solubility means the condition of being soluble. The term "each bead" refers to the beads containing an effective amount of one or more of said diltiazem salts as the active ingredient.	free base diltiazem be maintained, i.e., be held constant in every single bead. "Solubility" refers to the amount of material (expressed in units of mass) that are capable of being dissolved in an amount of solvent to give a saturated solution (expressed in units of volume) at a given temperature.

Andrx's construction ignores the stated purpose of the wetting agent and instead relies on extrinsic evidence for an understanding of the term "solubility" within term 6 of the '791 patent. Andrx asserts that solubility refers to "the amount of material (expressed in units of mass) that are capable of being dissolved in an amount of solvent to give a saturated solution (expressed in units of volume) at a given temperature." [D.I. 146, p. 20.] Thus, without any support, Andrx reads at least four limitations into the claims: (1) a specific amount of diltiazem expressed in units of mass; (2) a specific volume of solvent; (3) a specific temperature; and (4) a specific mathematical formula for calculating solubility. Further, the problem with Andrx's definition is that there is nothing in the intrinsic or extrinsic record that suggests that the inventors ever measured the actual numerical value for solubility of diltiazem, or further attempted to hold constant the solubility of diltiazem at a certain numerical value.

Andrx's argument that Biovail's construction would render the inventors' statements that the wetting agent controls solubility meaningless because, in Andrx's view, any material that is "slightly soluble" would always be in the "condition of being soluble," is nonsensical. Andrx provides no support that a "slightly soluble" material is in the "condition of being soluble." Indeed, if a substance is only slightly soluble, then it

will mostly exist in the solid state in the relevant admixture. Clearly, this is not the construction Biovail advocates. As explained in Biovail's opening brief [D.I. 147, *e.g.*, p. 5], and based on the plain language of the claims and numerous statements throughout the intrinsic record, the wetting agent of the '791 claims maintains the solubility of diltiazem, *i.e.*, maintains the diltiazem in an entirely dissolved (or liquid) state. If diltiazem is entirely in solution, then its solubility is maintained. If it precipitates out of solution (returns to the solid state), then its solubility is not maintained. This common sense construction does not rely on any particular numerical value for the solubility. Andrx's construction, in contrast, reads in a limitation that is unsupported by anything other than attorney argument.

Andrx also argues that Biovail's construction denigrates the action of the wetting agent, is at odds with the file history, and that Biovail is now turning its back on the critical wetting agent limitation by arguing that the claims cover a composition "so long as the wetting agent does not prevent gradual release of the drug." [D.I. 146, p. 23.] This is not Biovail's claim construction. Biovail's construction rests on the language of the claims, which provides that the wetting agent ensures the solubility of diltiazem is not adversely affected by the pH of the gastrointestinal tract. Further, Andrx asserts that Biovail's construction "conflates" solubility of a compound with release of a compound from a pharmaceutical composition. It is Andrx that conflates the analysis. The inventors made plain in the file history that the wetting agent does not permit the solubility of diltiazem to be affected and that "control affords a gradual release of Diltiazem in a relatively uniform manner over a period of about 24 hours." [5 A-71.]

Finally, Andrx accuses Biovail of "cherry-picking" from the file history

the inventors statement that "[t]his control [of the wetting agent] affords a gradual release of Diltiazem in a relatively uniform manner over a period of about 24 hours" and then purportedly changing its meaning. [D.I. 146, p. 23.] The meaning, however, does not change at all. As explained above, the wetting agent maintains the solubility of diltiazem, which "affords a gradual release of diltiazem in a relatively uniform manner over a period of about 24 hours." [5 A-71.]

7. "ensuring that the solubility of the Diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein"

'791 Claim Terms	Biovail's Construction	Andrx's Construction
"ensuring that the solubility of the diltiazem is unaffected by the pH of the gastrointestinal tract or other adverse conditions which the composition will meet therein"	Means the wetting agent does not permit the solubility of the diltiazem to be affected by the pH or other adverse conditions of the gastrointestinal tract in a manner that would prevent a gradual release of the drug in a relatively uniform manner. The term solubility means the condition of being soluble.	This limitation requires that the wetting agent be homogeneously admixed with the diltiazem salt ***so that the wetting agent will act in the composition to ensure the solubility of diltiazem is unaffected by the pH of the gastrointestinal tract*** or other adverse conditions the composition would meet if and when the composition is ultimately ingested by a patient. These adverse conditions can include changes in ionic strength, changes in temperature, or changes in pH. (emphasis added)

Andrx's construction arguments regarding term 7 of the '791 patent are incomprehensible, and, once again (as was the case with "effective amount") actually support an *in vivo* construction. Andrx's proposed construction concedes that the wetting agent "will act" to ensure that the solubility of diltiazem "is" unaffected by the pH of the gastrointestinal tract. Those words, like Andrx's construction of "effective amount" demand analysis of the beads *in vivo*, *i.e.*, after exposure to pH conditions of the

gastrointestinal tract, to determine whether the wetting agent has performed as required by the claims. Andrx cannot explain how one can evaluate this required function of the wetting agent by examination of the bead in the dry, pre-ingested state. In fact, one cannot.

8. "said beads being coated with a microporous membrane"

'791 Claim Terms	Biovail's Construction	Andrx's Construction
"said beads being coated with a microporous membrane"	Means that the beads have a microporous membrane.	This limitation refers to the membrane that is to be placed on the outside of each bead which is capable of forming micropores that contains the ingredients referred to later in the claim.

Andrx improperly characterizes the claim construction dispute. Andrx states that the dispute is whether (a) the beads are coated with a microporous membrane or (b) the microporous membrane is part of the bead itself (purportedly Biovail's construction). Biovail's construction, however, is not that the microporous membrane is part of the bead, but instead that the beads ***have a*** microporous membrane (which of course, encloses and contains the materials on the interior of the bead.) In other words, both parties agree that this membrane will be found as a distinct layer enclosing the remainder of the bead. To the extent that Andrx is arguing for additional requirements or limitations, its position is unsupported and nonsensical.

B. THE PROPER CONSTRUCTION OF THE '866 PATENT CLAIMS

Andrx's construction of the '866 patent improperly reads limitations into the claims and inappropriately asks this Court to make factual findings as to the meaning

and interpretation of USP and FDA guidance documents, *e.g.*, how one of ordinary skill in the art would understand USP 23, what conducting dissolution testing according to the methodology of USP 23 means to one of ordinary skill in the art, how one of ordinary skill in the art would understand FDA guidance documents, and what conducting *in vivo* clinical studies according to the FDA guidance documents means to one of ordinary skill in the art. *Cybor Corp. v. FAS Techs., Inc.*, 138 F.3d 1448, 1455-56 (Fed. Cir. 1998) (reaffirming the Supreme Court's unanimous decision in *Markman v. Westview Instruments, Inc*., 517 U.S. 370 (1996) that "claim construction is a pure issue of law" and does not involve subsidiary or underlying questions of fact.).

In addition, Andrx improperly tries to force its factual construction on the Court with unfounded assertions that Biovail's construction renders the claims indefinite. It is well-settled law that validity issues should not be considered during claim construction and therefore have no place in a Markman brief or hearing. *See Markman v. Westview Instruments, Inc*., 52 F.3d 967, 986 (Fed. Cir. 1995), *aff'd* , 517 U.S. 370 (1996), *citing Intervet Am., Inc. v. Kee-Vet Labs., Inc*., 887 F.2d 1050, 1053 (Fed. Cir. 1989) (matters which address claim validity are not relevant to claim construction and interpretation), *cited in Takata Corp.*, 1999 U.S. Dist. LEXIS at *29 n. 15; *Pharmastem Therapeutics, Inc. v. Viacell Inc.*, No. 02-148 (GMS), 2003 U.S. Dist. LEXIS 877 at *2 n. 1 (D. Del. Jan. 13, 2003) (refusing to address the defendants' indefiniteness argument during the Markman stage of the proceedings).

Finally, Andrx's construction of term 2 below would read out of the claims the embodiments found in Figures 9A and 9B of the '866 patent, which is improper. *Vitronics Corp.*, 90 F.3d at 1583 (a claim interpretation that excludes a

preferred embodiment "is rarely, if ever, correct and would require highly persuasive evidentiary support.").

1. "method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water . . . at 100 rpm in 900 ml of the buffered medium"[6]

'866 Claim Terms	Biovail's Construction	Andrx's Construction
"method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of water"	Plain meaning -- dissolution testing is conducted according to the methodology set forth in USP 23 at 100 rpm in 900 ml of water.	The dissolution testing is conducted according to USP 23, p. 1791 using Apparatus 1 (basket), 100 rpm, 900 ml of water as defined in the USP, employing the recited acceptance table, i.e the mean average % released of a minimum of six vessels with the detection of drug release being measured by UV absorption at the wavelength of 240 nm.

'866 Claim Terms	Biovail's Construction	Andrx's Construction
"method of United States Pharmacopoeia No. XXIII at 100 rpm in 900 ml of the buffered medium"	Plain meaning -- dissolution testing is conducted according to the methodology set forth in USP 23 at 100 rpm in 900 ml of the buffered medium.	The dissolution testing is conducted according to USP 23, p. 1791 using Apparatus 1 (basket), 100 rpm, 900 ml of an aqueous medium having a pH between 5.5 and 6.5 and a USP buffer such as 0.05 M phosphate buffer that is prepared according to USP methodology and further, employing the recited acceptance table, i.e., the mean average % released of a minimum of six vessels with the detection of drug release being measured by UV absorption at the wavelength of 240 nm.

[6] Biovail reprints Andrx's construction as it is set forth in the Final Joint Claim Construction Chart. As understood by Biovail, this is the construction that Andrx asks the Court to adopt. In its opening claim construction brief, Andrx's construction for the claim term regarding dissolution in water adds "which is Section <711>" and omits "with the detection of drug release being measured by UV absorption at the wavelength of 240 nm," and for the claim term regarding dissolution in buffered medium adds "which is Section <711>" and omits "of an aqueous medium having a pH between 5.5 and 6.5 and a USP buffer such as 0.05 M phosphate buffer that is prepared according to USP methodology."

Andrx's construction is a classic example of improperly reading limitations into the claims. Based on a hand-picked passage from the patent specification and on its own unsupported and misleading interpretation of USP 23, Andrx reads at least six limitations into term 1 of the '866 patent: (1) a specific section of USP 23; (2) use of a specific dissolution apparatus (Apparatus 1); (3) use of a specific type of buffer "prepared according to USP methodology"; (4) use of a specific acceptance table of USP 23; (5) use of a specific UV absorption wavelength for the dissolution testing; and (6) testing of a minimum of six tablets to "generate sufficiently reliable data." [D.I. 146, pp. 29-33.]

The passage from the specification on which Andrx relies to read the above limitations into the claims is as follows:

> Thus a 24-hour diltiazem preparation is provided wherein the Cmax of diltiazem in the blood is provided from about 10-15 hours after administration of a single dosage to a patient about 9-15 hours after multiple dosages over a number of days and displays the dissolution described above determined according to USP 23, page 1791 using Apparatus 1. [12 A-131 (12:42-48).]

When viewed in context, it is plain that this passage relates to particular embodiments discussed in the specification:

> According to another aspect of the invention, a method of treatment . . . comprising administration of a preparation of Diltiazem described above, to the patient in the evening for example at about 7:00-about 11:00 p.m. . . .
>
> According to ***another embodiment of the invention***, a method of treatment . . . comprising administration of a preparation which exhibits a higher bioavailability (***exceeding, for example, 25%***) when given at night compared to when given in the morning without food according to FDA guidelines or criteria . . .
>
> Thus a 24-hour diltiazem preparation is provided wherein the Cmax of diltiazem in the blood is provided from about 10-15 hours after administration of a single dosage to a

> patient about 9-15 hours after multiple dosages over a number of days and displays the dissolution described above determined according to USP 23, page 1791 using Apparatus 1. [12 A-131 (12:25-48) (emphasis added).]

These passages demonstrate that the inventors were describing various embodiments in this section of the patent specification. Specific requirements unique to those embodiments should not be read into the claims. *Vitronics Corp.*, 90 F.3d 1576 at 1583. For example, the inventors state that one embodiment concerns compositions for evening administration to patients between "7:00-about 11:00 p.m." [12 A-131 (12:25-29).] This is a specific requirement of that particular embodiment that Andrx has chosen to ignore because it does not help its argument. Just as the evening administration embodiment cannot be read into the claims, the specific embodiment that exhibits a dissolution pattern using Apparatus 1 should not be read into the claims.

Indeed, the only requirement of the '866 claims is that the dissolution testing be conducted according to the method of USP 23 at 100 rpm in 900 ml of water or buffered medium having a pH between about 5.5 and about 6.5. It is improper to read a requirement from a specific embodiment into the claims. *Phillips*, 415 F.3d at 1323.

Andrx purposefully disregards the language of the patent specification at Column 5, lines 28-61, which is identical to the language of the patent claims, because it does not include any of the limitations that Andrx seeks to read into the claims:

> Column 5:28-61 of the specification does not identify or refer to any particular page or section of the USP 23, and does not mention any particular apparatus to be used.
> [D.I. 146, p. 30.]

Andrx's stated basis for reading into the claims the "rules for interpretation and acceptance of results within Section <711> of USP 23," is that they are an "integral part of the testing procedure because they reflect the USP's judgment of

when and under what circumstances data generated by its own testing protocol are meaningful." [D.I. 146, p. 32.] This Court should disregard Andrx's attorney arguments interpreting USP 23, and should reject Andrx's attempt to conflate the Court's claim construction analysis with factual determinations as to the meaning and interpretation of USP 23. *Cybor Corp.*, 138 F.3d at 1455-56 (reaffirming the Supreme Court's unanimous decision in *Markman v. Westview Instruments, Inc*., 517 U.S. 370 (1996) that "claim construction is a pure issue of law" and does not involve subsidiary or underlying questions of fact.).[7]

Andrx is clearly trying to engineer a non-infringement driven claim construction that improperly asks this Court to make factual findings as to what certain extrinsic documents require. Whether or not the particular dissolution data for Andrx's product meets the requirements of this claim is a factual determination that should be left for the infringement analysis case. *Cybor Corp.*, 138 F.3d at 1455-56.

Andrx's construction violates several maxims of claim construction. It is entirely improper to construe a claim based on extrinsic evidence, to incorporate factual determinations into the claim construction process, and to read limitations into claims from the specification (and other, clearly extrinsic) sources. *Phillips*, 415 F.3d at 1318-1321.

In addition, for reasons Andrx does not explain, Andrx cites the inventors'

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[7] Indeed, the danger of allowing such determinations during claim construction is evidenced by Andrx's requests to read into the claims the "acceptance criteria" at page 33 of Andrx's answering brief. [D.I. 146.] According to Andrx's own unsupported and misleading interpretation of USP 23, the "acceptance criteria" is directed to dissolution requirements for a given product having a USP monograph, and not a patent claim. [*Id*., p. 33, n. 7.]

May 3, 2001 submission to the Patent Office as support that the invention requires use of Apparatus 1. [D.I. 146, p. 29.] The cited submission makes plain, however, that the invention is not limited to use of a specific dissolution apparatus. There the inventors argued that the dissolution rates of European Patent Application 0 856 313 ("EP '313") -- measured according to "U.S. Pharmacopeia XXI Paddle Method [Apparatus 2] in 0.05 M KCl at pH 7.0 and at 100 r.p.m." (*see e.g.*, 17 A-562-563 (7:58-8:1), A-568 (13:10-11), A-570 (15:19-20), A-571 (16:36-37), A-572 (17:23-24)) -- are **different** from the invention because EP '313 uses buffered medium having a pH of 7.0, which is outside the claimed buffered medium having a pH "between about 5.5 and about 6.5":

> Further, the determination of the dissolution rates in '313 is in accordance with U.S. Pharmacopeia XXI in 0.05M KCl at pH 7.0 (not in accordance with Applicant's claimed procedure). [13 A-172.]

The inventors distinguished the data based on the conditions like the pH of the buffer used in the prior art reference, and never argued or suggested that the use of Apparatus 2 in EP '313 distinguished that document from their invention.

Further, Andrx improperly asks the Court to consider the validity of the '866 patent claims in the context of claim construction. Specifically, Andrx criticizes Biovail's construction, which rests firmly on the plain and ordinary meaning of the words of the claim, as indefinite. [D.I. 146, p. 30.] However, even if Biovail's construction was indefinite (which it is not), this is a validity argument. As discussed above, it is well-settled law that it is improper to consider a claim's validity during claim construction.

Moreover, in the case on which Andrx relies, *Rhodia Chimie v. PPG Indus. Inc.*, 402 F.3d 1371 (Fed. Cir. 2005), the Federal Circuit did not construe a claim to avoid indefiniteness as Andrx suggests. [D.I. 146, p. 30.] *Rhodia Chimie* concerned

an ambiguous claim term that was resolved with reference to information within the patent specification. *Rhodia Chimie*, 402 F.3d at 1378. There is no mention of an "indefinite" claim in *Rhodia Chimie*, or the need to consider the validity of a claim term in the context of claim construction. *Id.* at 1377-80.

Andrx also inconsistently argues that section 711 of USP 23 is intrinsic evidence and that other sections of USP 23 such as section 724 and the supplements to USP 23 are extrinsic evidence. [D.I. 146, p. 30.] This makes no sense because the patent specification at Column 5, lines 28-61 refers to USP 23 without limitation to a particular section, and at the time of the filing of the '866 invention, USP 23 and its supplements (through number 10) were all available to one of ordinary skill in the art. Thus, all of USP 23 must stand or fall together as either intrinsic or extrinsic evidence.

Andrx also points to the USP monograph for diltiazem hydrochloride tablets in USP 23 -- an entirely different product from Cardizem® LA -- and argues, without explanation, that it is "a red herring." [D.I. 146, p. 31; 20 A-797.] Andrx then makes a convoluted analogy between the '866 patent claims and the USP monograph for diltiazem hydrochloride tablets based on its unsupported and misleading interpretations of USP 23. [D.I. 146, p. 31.] Andrx's analogy requires the Court to adopt Andrx's analysis and misleading interpretation of the USP monograph for diltiazem hydrochloride tablets and to apply that same analysis and interpretation to the construction of the '866 patent claims. This is improper and makes no sense because the USP monograph and the '866 patent claims are two very different things that serve two very different purposes. Biovail agrees that the extrinsic evidence of this USP evidence is not relevant to the Court's claim construction. In any event, this monograph, which relies on testing

in Apparatus 2, certainly does not support Andrx's efforts to read Apparatus 1 into the claims.

In stark contrast to Andrx's construction, Biovail's construction rests on the plain language of the '866 patent claims, *i.e.*, *in vitro* release (or dissolution) is measured according to the methodology of USP 23 at 100 rpm in 900 ml of water or at 100 rpm in 900 ml of buffered medium having a pH between about 5.5 and about 6.5. Whether specific data presented as infringement proofs in this case meet the requirements of USP 23 is a question for the finder of fact, and does not belong in the purely legal claim construction analysis.

2. "higher bioavailability when given at night compared to when given in the morning without food according to FDA guidelines or criteria"[8]

'866 Claim Terms	Biovail's Construction	Andrx's Construction
"higher bioavailability when given at night compared to when given in the morning without food according to FDA guidelines or criteria"	means the composition gives a night vs. day dosing ratio of >1 for AUC and Cmax when given without food.	"higher bioavailability" refers to a formulation when administered at night under appropriate test parameters that exhibits an AUC and a Cmax that exceed the 90% confidence interval as determined according to FDA guidelines of the AUC and Cmax of the same formulation administered in the morning under appropriate test parameters. The appropriate test parameters are defined in "GUIDANCE ORAL EXTENDED (CONTROLLED) RELEASE DOSAGE FORMS IN VIVO BIOEQUIVALENCE AND IN VITRO DISSOLUTION TESTING" prepared

[8] Biovail reprints Andrx's construction as it is set forth in the Final Joint Claim Construction Chart. As understood by Biovail, this is the construction that Andrx asks the Court to adopt. In its opening claim construction brief, Andrx's construction for the claim term adds language and omits several portions of its construction.

		under 21 CFR 10.90(b)(9) by Shrikant V. Dighe, Ph.D., Director, Division of Bioequivalence Office of Generic Drugs dated Sep. 3, 1993 and concurred by Roger L. Williams, M.D., Director, Office of Generic Drugs, Center for Drug Development Research dated Sep. 4, 1993. The data from the study should be analyzed as defined in "GUIDANCE STATISTICAL PROCEDURES FOR BIOEQUIVALENCE STUDIES USING A STANDARD TWO-TREATMENT CROSSOVER DESIGN" prepared under 21 CFR 10.90(b) by Mei-Ling Chem, Ph.D., Division of Bioequivalence Review Branch II dated June 12, 1992 and Rabindra Patnaik, Ph.D., Division of Bioequivalence Review Branch II dated June 26, 1992, approved by Shirkant V. Dighe, Ph.D., Director, Division of Bioequivalence dated June 29, 1992 and concurred by Roger L. Williams, M.D., Director, Office of Generic Drugs dated June 29, 1992.

The parties agree that the word "bioavailability" in term 2 of the '866 patent refers to AUC and Cmax. The first disagreement lies in Andrx's attempt to read into the claims specific "pharmacokinetic test protocols" purportedly in the FDA guidance documents referred to at Column 8, lines 13-34 of the patent specification. Andrx not only asks this Court to read limitations into the claims, it once again asks the Court in the context of claim construction to make factual determinations as to the meaning and interpretation of the FDA guidelines, which is improper. *Cybor Corp.*, 138 F.3d at 1455-56.

Andrx's argument that Biovail declines to take any position as to "the protocol" to be used to generate AUC and Cmax is misleading, because it presumes that there is a specific protocol, *i.e.*, a specific *in vivo* study that must be used to generate

AUC and Cmax. [D.I. 146, p. 35.] The FDA guidance documents cited in the patent specification do not identify specific test protocols that must be followed. The FDA guidance documents, however, only provide examples of *in vivo* studies that could be performed:

> . . . The above objectives are ***generally*** met by the following three in vivo studies:
>
> A single dose, randomized, two-period, two-treatment, two-sequence crossover study under fasting conditions, comparing equal doses of the test and reference products.
>
> A single dose, randomized, three-treatment, three-period, six sequence, crossover, limited food effects study, comparing equal doses of the test product administered under fasting conditions with those of the test and reference products administered immediately after a standard breakfast.
>
> A multiple dose, steady state, randomized, two-treatment, two-period, two-sequence crossover study under fasting conditions comparing equal doses of the test and reference formulations. For safety reasons, this study may be performed in the non-fasting state. Applicants are encouraged to submit a study protocol describing the safety considerations requiring deviation from the fasting state to the Division of Bioequivalence for review prior to execution of the study. [18 A-753-754 (emphasis added).]

But more to the point, as was the case above, whether particular data meets the claim limitation is an issue for the finder of fact, and is not a claim construction issue. *See Cybor Corp.*, 138 F.3d at 1455-56.

The second disagreement lies in Andrx's attempt to replace the plain and ordinary meaning of "higher bioavailability" with its misleading, unsupported and entirely factual interpretation of the FDA guidance documents. Under Andrx's construction, "higher bioavailability" means that AUC and Cmax for the formulation when administered at night exceed the 90% confidence interval. Stated differently, the

AUC and Cmax of the formulation when given at night is so high that the formulation is not bioequivalent when given in the morning without food. There is no intrinsic support for this construction. Moreover, Andrx's construction is inconsistent with the plain and ordinary meaning of "higher bioavailability," *i.e.*, the ratio of night to morning administration is greater than one.

As explained in Biovail's opening brief [D.I. 147, pp. 30-33], this construction is supported by the patent specification and prosecution history. For example, during prosecution of the patent, the inventors stated "[t]he LA formulation provides for a much higher bioavailability ***(both AUC and Cmax are > than 1)***". [16 A-482; 17 A-659, A-664 (emphasis added).] Andrx wrongly, attempts to discredit these statements on the purported basis that they did not result in allowance of the patent. *See Microsoft Corp. v. Multi-Tech Sys., Inc*., 357 F.3d 1340, 1350 (Fed. Cir. 2004) ("a patentee's statements during prosecution, whether relied on by the examiner or not, are relevant to claim interpretation"); *Laitram Corp. v. Morehouse Indus., Inc*., 143 F.3d 1456, 1462 (Fed. Cir. 1998) (the argument that a statement "was not relied upon by the examiner and is therefore irrelevant to claim construction, is not sustainable under our case law"); *E.I. Du Pont De Nemours & Co. v. Phillips Petroleum Co*., 849 F.2d 1430, 1438 (Fed. Cir. 1988) ("Regardless of the examiner's motives, arguments made during prosecution shed light on what the applicant meant by its various terms.").

Further, Andrx's construction would read out of the claims the embodiment of the invention disclosed in Figures 9A and 9B. *Vitronics Corp.*, 90 F.3d at 1583 (a claim interpretation that excludes a preferred embodiment "is rarely, if ever, correct and would require highly persuasive evidentiary support."). The formulation

disclosed in Figures 9A and 9B was administered at night and in the morning without food according to FDA guidelines. [12 A-120 -121.] This embodiment would not satisfy the limitations that Andrx attempts to graft into claim 1 from its unsupported factual analysis of extrinsic FDA documents.

3. "bioequivalence when given in the morning with or without food according to the same FDA guidelines or criteria"[9]

'866 Claim Terms	Biovail's Construction	Andrx's Construction
"bioequivalence when given in the morning with or without food according to the same FDA guidelines or criteria"	Plain meaning -- food does not render the composition bioinequivalent when the composition is given in the morning with or without food.	"bioequivalence" refers to a formulation when given in the morning with or without food under appropriate test parameters that exhibits an AUC and a Cmax within the 90% confidence interval as determined according to FDA guidelines of the AUC and Cmax of the same formulation administered in the morning under appropriate test parameters. The appropriate test parameters are defined in "GUIDANCE ORAL EXTENDED (CONTROLLED) RELEASE DOSAGE FORMS IN VIVO BIOEQUIVALENCE AND IN VITRO DISSOLUTION TESTING" prepared under 21 CFR 10.90(b)(9) by Shrikant V. Dighe, Ph.D., Director, Division of Bioequivalence Office of Generic Drugs dated Sep. 3, 1993 and concurred by Roger L. Williams, M.D., Director, Office of Generic Drugs, Center for Drug Development Research dated Sep. 4, 1993. The data from the study should be analyzed as defined in "GUIDANCE

[9] Biovail reprints Andrx's construction as it is set forth in the Final Joint Claim Construction Chart. As understood by Biovail, this is the construction that Andrx asks the Court to adopt. In its opening claim construction brief, Andrx's construction for the claim term adds language and omits several portions of its construction.

		STATISTICAL PROCEDURES FOR BIOEQUIVALENCE STUDIES USING A STANDARD TWO-TREATMENT CROSSOVER DESIGN" prepared under 21 CFR 10.90(b) by Mei-Ling Chem, Ph.D., Division of Bioequivalence Review Branch II dated June 12, 1992 and Rabindra Patnaik, Ph.D., Division of Bioequivalence Review Branch II dated June 26, 1992, approved by Shirkant V. Dighe, Ph.D., Director, Division of Bioequivalence dated June 29, 1992 and concurred by Roger L. Williams, M.D., Director, Office of Generic Drugs dated June 29, 1992.

Similar to term 2 of the '866 patent, Andrx's construction seeks to read into the claims specific "pharmacokinetic test protocols" purportedly found in the FDA guidance documents referred to at Column 8, lines 13-34 of the patent specification. Once again, Andrx asks the Court in the context of claim construction to make factual determinations as to the meaning and interpretation of those guidance documents. For the reasons explained above as to term 2 of the '866 patent, this is improper and incorrect.

Biovail's construction is based on the plain meaning of the claim language. The plain words of the claim state that when the composition is given in the morning with or without food the formulation is bioequivalent, *i.e.*, meets the FDA guidelines or criteria for bioequivalence. Stated differently, food does not render the composition bioinequivalent when the composition is given in the morning with or without food. Whether particular proofs satisfy this limitation will again be in the province of the finder of fact. There is no basis to read in a half page worth of limitations that appear nowhere in the intrinsic record, as Andrx does. Moreover, Andrx accusation

that Biovail purportedly made up the term "bioinequivalent" is unfounded. [D.I. 146, p. 38.] The FDA itself has used the term "bioinequivalence" in its "Guidance for Industry" publications:

> We recommend that dissolution testing is also used to (1) provide process control and quality assurance, and (2) assess whether further BE studies relative to minor postapproval changes be conducted, where dissolution can function as a signal of ***bioinequivalence***. [24 A-886. (emphasis added).]

CONCLUSION

For the foregoing reasons, and the reasons set forth in Biovail's opening claim construction brief, Biovail respectfully requests that the Court adopt its constructions of the disputed claim terms of the '791 and '866 patents.

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April 24, 2007

CERTIFICATE OF SERVICE

I, the undersigned, hereby certify that on April 24, 2007, I electronically filed the foregoing with the Clerk of the Court using CM/ECF, which will send notification of such filing(s) to the following:

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